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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
CALAMITA, HEATHER	

ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 06/23/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/910,383	NALLUR ET AL.	
	Examiner	Art Unit	
	Heather G. Calamita, Ph.D.	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 October 2001*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-73* is/are pending in the application.

4a) Of the above claim(s) *63-67* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-62 and 68-73* is/are rejected.

7)☒ Claim(s) *30 and 37* is/are objected to.

8)☒ Claim(s) *1-73* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *18 October 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-62 and 68-73, drawn to method of amplifying mRNA, classified in 435, subclass 6.

II. Claims 63-67, drawn to a kit and composition for amplifying mRNA, classified in class 435, subclass 6.

The inventions are distinct, each from the other because:

Inventions Group I and Group II are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the kit may be used in amplification processes such as rolling circle replication or reverse transcription PCR.

Because these inventions are distinct for the reasons given above and the search required for each Group is not required for the other Groups, restriction for examination purposes as indicated is proper.

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of In re Ochiai, In re Brouwer and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on

the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.** Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

2. During a telephone conversation with Robert Hodges on May 4, 2004, a provisional election was made with traverse to prosecute the invention group I claims 1-62 and 68-73. Affirmation of this election must be made by applicant in replying to this Office action. Claims 63-67 are withdrawn from further consideration by the examiner, 37 CFR 1.14(b), as being drawn to a non-elected invention.

Claim Objections

3. Claims 30 and 37 are objected to because of the following informalities: In claim 30 "phytoerythrin" is misspelled. Claim 37 is a duplicates claim 2. Appropriate correction is required.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 16-17 recites the limitation "half probe" in lines 2 and 3 of the claims respectively. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1, 4-15, 18-29, 31-36, 40-45, 62, 68, 70-72 are rejected under 35 U.S.C. 102(a) as being anticipated by Alsmadi et al.(USPN 6,573,051 B2 06/03/2003).

Alsmadi et al. teach a method of amplifying RNA mixing RT primers with a nucleic acid sample and reverse transcribing to produce cDNA strands each comprising one of the RT primers, wherein each primer comprises a reverse transcription primer portion (see whole document, especially, col. 35 lines 33-35). They also teach hybridizing the cDNA strands to a set of capture probes (see col. 12 lines 13-22). They teach mixing one or more rolling circle replication primers with the cDNA strands under conditions that promote association of the cDNA strands with the rolling circle replication primers, wherein the rolling circle replication primers each comprise a capture tag, and wherein association occurs via the capture tag. They teach mixing one or more amplification target circles with the rolling circle replication primers under conditions that promote association of the rolling circle replication primers with the amplification target circles wherein replication of the amplification target circles results in the formation of tandem sequence DNA (see col. 13 lines 61-67, col. 14 lines 1-9, 11-17, col. 35 lines 35-59). Alsmadi et al. teach the capture probes immobilized on a substrate, in an array, and they also teaches the capture probes immobilized via a capture tag coupled to the capture probes (see col. 28 lines 4-5, 8-12, col. 27 lines 50-55). They further teach each capture probe having a sequence matching all or a portion of the sequence of messenger RNA molecules of interest (see col. 6 line 13, col. 28 lines 8-17). They further teach a set of capture probes collectively comprise sequence matching all or a portion of the sequence of a plurality of different messenger RNA molecules derived from or present in cells from multiple sources of interest and that are associated with a condition or disease state of the cells or source of interest (see col. 34 lines 30-59, col. 39 lines 56-63). They teach a plurality of different mRNA molecules that make up a set of mRNA molecules representing a catalog of mRNA molecules from a source of interest (see col. 33 lines 63-67). They teach the ends of the capture probes are extendable when a cDNA strand is hybridized to the capture probe (see col. 40 lines 13-16). They teach mixing a secondary DNA strand displacement

primer with the amplification target circles and incubating under conditions tat promote hybridization of the TS-DNA and the secondary DNA strand displacement primer and replication of the TS-DNA. They additionally teach simultaneous with amplification, mixing a tertiary DNA strand displacement primer with the amplification target circles (see col. 36). They also teach detecting the TS-DNA where the TS-DNA indicates that the corresponding mRNA was present in the sample (see col. 35 lines 26-32). They teach detecting the TS-DNA while in association with the capture probes (see col. 28 lines 4-18). They teach the identity of the capture probe associated with the TS-DNA indicates the identity of the corresponding mRNA molecule (see col. 28 lines 4-18, col. 38 lines 20-35). Furthermore, they teach TS-DNA is detected at the site where the capture probe is located and the location of the capture probe indicates the identity of the corresponding mRNA molecule (see col. 38 lines 20-35). They additionally teach detection is mediated by detection probes or by a detection label incorporated in the TS-DNA and the detection label is a ligand that is either biotin or BrdU (see col. 39 lines 14-27). They teach the ligand is BrdU wherein the TS-DNA is detected by associating an anti-BrdU antibody with the TS-DNA and detecting the anti-BrdU antibody (see col. 39 lines 14-27). Alsmadi et al. teach the anti-BrdU antibody comprises a label wherein the anti-BrdU antibody is detected by detecting the label and they teach the label is a fluorophore (see col. 26 lines 50-60). They also teach hybridizing a set of detection probes with TS-DNA and detecting a plurality of different sequences present in the TS-DNA (see col. 40 lines 50-60). They teach the TS-DNA is collapsed using collapsing probes and at least one of the collapsing probes is a collapsing detection probe (see col. 39 line 5) They further teach the TS-DNA is collapsed by mixing the collapsing probes with the TS-DNA and hybridizing the collapsing probes and the TS-DNA and simultaneously mixing detection probes with the TS-DNA under conditions to promote hybridization between the TS-DNA and the detection probes. They teach the detection probes as ligands, haptens or both coupled to or incorporated into oligonucleotides (see col. 44 lines 4-15, 42-49). Alsmadi et al. teach teach cDNA strands comprise capture tags selected from the group consisting of biotin, digoxigenin,

bromodeoxyuridine, or other hapten (see col. 43 lines 55-56). They also teach the association between the rolling circle replication primers with the amplification target circles as being covalent or non-covalent (see col. 34 lines 61-66). They teach association between a protein and a nucleic acid and between two proteins (see col. 6 lines 9-16, col. 41 lines 59-67, col. 42 lines 1-16).

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 3 is rejected under 35 U.S.C. 103(a) as being unpatentable over Alsmadi et al.(USPN 6,573,051 B2 06/03/2003) in view of Wei et al. (US 2003/0032014 A1 02/13/2003).

The teachings of Alsmadi et al. are described previously.

Alsmadi et al. do not teach the reverse transcription primer portion of each RT primer comprises a poly T.

Wei et al. teach an RT primer that has a poly T (see paragraph 0037 line 4).

One of ordinary skill in the art at the time the invention was made one would have been motivated to apply Wei's poly T RT primers to Alsmadi's method of amplifying target nucleic acids to achieve primer binding only to the poly A tail of the mRNA. It would have been prima facie obvious to apply Wei's poly T primers to Alsmadi's method of amplifying nucleic acids in order to achieve the expected advantage of amplifying a greater number of full transcripts without genomic DNA contamination, as the poly a tail is located at the beginning of the gene.

5. Claims 16-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Alsmadi et al.(USPN 6,573,051 B2 06/03/2003) in view of Lizardi (US 2003/0032024 A1 02/13/2003).

The teachings of Alsmadi et al. are described previously.

Alsmadi et al. do not teach mixing one or more half probes with the cDNA strands wherein each half probe is designed to hybridize to a cDNA strand adjacent to where a capture probe hybridizes, ligating half probes and capture probes hybridized. They also do not teach following ligation, incubating the capture probes at a temperature above the melting temperature of the capture probe but below the melting temperature of the ligated capture probe/half probe.

Lizardi teaches mixing one or more half probes (gap oligonucleotides) with the cDNA strands wherein each half probe is designed to hybridize to a cDNA strand adjacent to where a capture probe hybridizes, ligating the half probes and capture probes hybridized, and after ligation , incubating the capture probes at a temperature above the melting temperature of the capture probe but below the melting temperature of the ligated capture probe/half probe (see whole document, especially paragraph 0195).

One of ordinary skill in the art at the time the invention was made one would have been motivated to apply Lizardi's method of mixing gap oligonucleotides with capture probes and incubating the mixture in a temperature dependent manner to Alsmadi's method of amplifying target nucleic acids to achieve more selective target discrimination. Lizardi states using gap oligonucleotides enhance target dependency in LCR and this can be adapted for use in LM-RCA, and this method enhances target discrimination. It would have been prima facie obvious to apply Lizardi's use of gap oligonucleotides to Alsmadi's method of amplifying nucleic acids in order to achieve the expected advantage of enhancing target nucleic acid discrimination.

6. Claim 30 is rejected under 35 U.S.C. 103(a) as being unpatentable over Alsmadi et al.(USPN 6,573,051 B2 06/03/2003) in view of Waggoner et al. (USPN 6,008,373 12/28/1999).

The teachings of Alsmadi et al. are described previously.

Alsmadi et al. do not teach phycoerythrin as a fluorophore.

Waggoner et al. teach using phycoerythrin as a fluorophore in the detection label on an antibody (see col. 21 line 64).

One of ordinary skill in the art at the time the invention was made one would have been motivated to apply Waggoner's method of using phycoerythrin as a detection label to Alsmadi's method of amplifying target nucleic acids to achieve a detection signal that provides fluorescence that is relatively free of interference from other biological materials and provides a multicolor fluorescence emission using a single wavelength excitation. Waggoner states that phycoerythrin is advantageous because it is low molecular weight and provides a multicolor fluorescence emission using a single wavelength excitation (see col. 2 lines 28-30). It would have been prima facie obvious to apply Waggoner's use of Phycoerythrin to Alsmadi's method of amplifying nucleic acids in order to achieve the expected advantage of a label that has a low molecular weight and provides a multicolor fluorescence emission from a single excitation wavelength.

7. Claims 2, 48-55, 69, are rejected under 35 U.S.C. 103(a) as being unpatentable over Alsmadi et al.(USPN 6,573,051 B2 06/03/2003) in view of Cao et al. (US 2002/0120409 A1 08/29/2002).

The teachings of Alsmadi et al. are described previously.

Alsmadi et al. do not teach fragmenting and labeling cDNA strands to form labeled fragmented cDNA. They do not teach the RT primer comprising a capture tag of biotin and the cDNA strands having the capture tag.

Cao et al. teach fragmented cDNA in a method to amplify mRNA (see claim 1 page 8). They also teach the RT primer comprising a capture tag of biotin and the cDNA strands having the capture tag (see paragraphs 0045-0049).

One of ordinary skill in the art at the time the invention was made one would have been motivated to apply Cao's method of fragmenting and labeling cDNA to Alsmadi's method of amplifying target nucleic acids to obtain labeled cDNA fragments that are used in assessing gene expression. It would have been prima facie obvious to apply Cao's labeled cDNA fragments to Alsmadi's method of amplifying nucleic acids in order to achieve the expected advantage of using the labeled cDNA fragments in gene expression arrays.

8. Claims 56-61 are rejected under 35 U.S.C. 103(a) as being unpatentable over Alsmadi et al.(USPN 6,573,051 B2 06/03/2003) in view of Shoemaker et al. (USPN 6,713257 B2 03/30/2004). 02/13/2003).

The teachings of Alsmadi et al. are described previously.

Alsmadi et al. do not teach a capture tag derived from allyl amine dUTP.

Shoemaker et al. teaches using an amino-allyl dUTP in labeling cDNA (see col. 34 line 8).

One of ordinary skill in the art at the time the invention was made one would have been motivated to apply Shoemaker's method of labeling cDNA to Alsmadi's method of amplifying target nucleic acids to obtain labeled cDNA that are used in assessing gene expression. It would have been prima facie obvious to apply Shoemaker's labeled cDNA fragments to Alsmadi's method of amplifying nucleic acids in order to achieve the expected advantage of incorporating a detectible fluorescent label into the cDNA of interest.

9. Claims 73 is rejected under 35 U.S.C. 103(a) as being unpatentable over Alsmadi et al.(USPN 6,573,051 B2 06/03/2003) and Waggoner et al. (USPN 6,008,373 12/28/1999) in view of Cao et al. (US 2002/0120409 A1 08/29/2002).

The teachings and suggestions of Alsmadi et al. and Waggoner et al. are described previously.

Alsmadi et al. do not teach the RT primer comprising a capture tag of biotin and the cDNA strands having the capture tag.

Cao et al. teach the RT primer comprising a capture tag of biotin and the cDNA strands having the capture tag (see paragraphs 0045-0049).

One of ordinary skill in the art at the time the invention was made one would have been motivated to apply Cao's method of labeling cDNA to the combined invention of Alsmadi and Waggoner's method of amplifying target nucleic acids to obtain labeled cDNA fragments that are used in assessing gene expression. It would have been prima facie obvious to apply Cao's labeled cDNA fragments to the combination of Alsmadi and Waggoner's method of amplifying nucleic acids in order to achieve the expected advantage of using the labeled cDNA in gene expression arrays.

Summary

10. No claims were allowed.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Heather G. Calamita, Ph.D. whose telephone number is 571.272.2876 and whose e-mail address is heather.calamita@uspto.gov. However, the office cannot guarantee security through the e-mail system nor should official papers be transmitted through this route. The examiner can normally be reached on weekdays 7:30 A.M. - 4:00 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571.272.0782. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

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PRIMARY EXAMINER
6/21/04